The correspondence section is a public forum and, as such, is not peer-reviewed. EHP *is not responsible for the accuracy, currency, or reliability of personal opinion expressed herein; it is the sole responsibility of the authors.* EHP *neither endorses nor disputes their published commentary.*

C-Reactive Protein Levels in Pregnancy

http://dx.doi.org/10.1289/ehp.1205429

van den Hooven et al. (2012) found a nonsignificant association between high levels of maternal and fetal C-reactive protein (CRP) and exposure to air pollution when they examined the correlation of CRP levels with inflammation and obstetric morbidity. The authors reported that elevated fetal CRP levels at delivery were associated with higher long-term average maternal exposure to PM_{10} (particulate matter ≤ 10 μm in aerodynamic diameter) and NO_2 (nitrogen dioxide). Other studies have reported that neither preeclampsia (Kristensen et al. 2009) nor pregnancy loss (Boggess et al. 2005) is associated with a systemic inflammation as reflected by CRP levels. However, van den Hooven et al. (2012) insisted that exposure to air pollution may lead to systemic inflammation in pregnancy. Although this statement is defensible, the confounding results regarding CRP levels should be clarified.

CRP is accepted as a good marker of acute inflammation, particularly within infection, but its value in chronic inflammation depends on the inflammation pathway involved and the underlying process. In an examination of autoimmune inflammatory responses triggered by the indoor environment in sick buildings, CRP was < 0.1 mg/dL (normal range, 0.1–0.5 mg/dL) in 27% of patients (Blasco 2011). Interestingly, 13% of patients had suffered miscarriages. CRP may be low or typically very low during a flare-up of some connective tissue disorders, such as systemic lupus erythematosus (SLE) or undifferentiated connective tissue disease. The erythrocyte sedimentation rate more accurately reflects SLE disease activity in patients without associated infection. Therefore, the presence of normal or low CRP levels does not guarantee the absence of inflammation or a positive pregnancy outcome. It would be interesting to assess possible individual immune susceptibility markers and other markers, such as autoantibodies or tumor necrosis factor α, in future studies of systemic inflammation induced by air pollutants during pregnancy.

The author declares he has no actual or potential competing financial interests.

Luis Miguel Blasco
Unidad de Alta Resolución Hospitalaría
Hospital Marqués de Valdecilla
Santander, Spain
E-mail: grullus99@yahoo.es

References

Blasco LM. 2011. Sick building syndrome and autoimmunity [Letter]. Lupus 20:544–546.

Boggess KA, Lieff S, Murtha AP, Moss K, Jared H, Beck J, et al. 2005. Maternal serum C-reactive protein concentration early in pregnancy and subsequent pregnancy loss. Am J Perinatol 22:299–304.

Kristensen K, Wide-Swensson D, Lindstrom V, Schmidt C, Grubb A, Strevens H. 2009. Serum amyloid a protein and C-reactive protein in normal pregnancy and preeclampsia. Gynecol Obstet Invest 67:275–280.

van den Hooven EH, de Kluizenaar Y, Pierik FH, Hofman A, van Ratingen SW, Zandveld PY, et al. 2012. Chronic air pollution exposure during pregnancy and maternal and fetal C-reactive protein levels: the Generation R Study. Environ Health Perspect 120:746–751.

Editor's note: In accordance with journal policy, van den Hooven et al. were asked whether they wanted to respond to this letter, but they chose not to do so.

Use of Meta-analyses by IARC Working Groups

http://dx.doi.org/10.1289/ehp.1205397

In their letter, Kogevinas and Pearce (2012) suggested that meta-analyses should be more routinely prepared for the evaluations of the International Agency for Research on Cancer (IARC) Monographs program. We concur that meta-analyses are useful in many cases, but there are also counter examples where they have not been useful. For example, when Kogevinas et al. (1998) reviewed the carcinogenicity of cancer hazards in the rubber-manufacturing industry, they argued against using meta-analytic techniques because of the heterogeneity of exposure circumstances within and between manufacturing plants and differences of exposure classifications used in the studies. They concluded that a single summary risk estimate would be uninformative. Based on their systematic narrative review, the authors concluded that there is an increased risk of neoplasms of the urinary bladder, lung, and larynx and an increased risk of leukemia (Kogevinas et al. (1998). In contrast, Alder et al. (2006) performed a meta-analysis of cancer occurrence among workers in the rubber-manufacturing industry. Based on summary estimates for the entire rubber industry and two major sectors of this industry, these authors concluded that excesses other than for leukemia were not substantiated by their synthetic meta-analysis (Alder et al. 2006). After reviewing all the pertinent studies, a later IARC Working Group concluded that there is sufficient evidence for an increased risk of several types of cancer in rubber manufacturing (Baan et al. 2009).

In contrast, when the IARC Working Group for Volume 98 reviewed the evidence on shift work and cancer, a published meta-analysis had reported a statistically significantly increased risk for breast cancer among women who regularly worked the night shift (Megdal et al. 2005). Nevertheless, the IARC Working Group concluded that there was only limited evidence for carcinogenicity in humans (IARC 2010).

In the context of the Volume 98 Monographs meeting, the Working Group performed a meta-analysis and concluded that there was sufficient evidence for the carcinogenicity of exposures as a painter (IARC 2010). In preparation for the Volume 100 series of the *IARC Monographs*, this meta-analysis was further developed, taking into account studies published after the Volume 98 meeting (Guha et al. 2010). This meta-analysis and another one (Bachand et al. 2010) were available to the Working Group for Volume 100F. Bachand et al. (2010) did not provide results by duration of employment or for nonsmokers, but they argued that the increased risks could be due to residual confounding. After reviewing all published evidence, the IARC Working Group reconfirmed the carcinogenicity of exposures as a painter.

In general, during the last two decades meta-analyses have become more widely used in epidemiology, and the 2006 amendment of the IARC Preamble now specifically mentions the possibility of premeeting and ad hoc meta-analyses during the course of a Monograph meeting (IARC 2006). In practice, this has been done even earlier, for example, when the Working Group for Volume 83 updated a published meta-analysis on involuntary smoking and lung cancer (IARC 2004). Anticipating scenarios as described above, the Preamble (IARC 2006) stresses the need "that the same criteria for data quality be applied as those that would be applied to individual studies."

Kogevinas and Pearce (2012) referred to a recently published meta-analysis for asbestos and ovarian cancer that we coauthored (Camargo et al. 2011). Interestingly, another meta-analysis of this same question was published by Reid et al. (2011). Whereas our meta-analysis focused on occupational cohorts with well-documented exposure to asbestos and identified almost twice as many cases from occupational cohorts, Reid et al. also included environmental and household exposures as well as linkage and case–control studies. Nevertheless, both meta-analyses reported increased risks overall and in most stratified analyses. However, while Reid et al. (2011) believed that increased risks may be